

09/720841

PCT/GB99/02042

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WO 00/00500

The erythromycin PKS

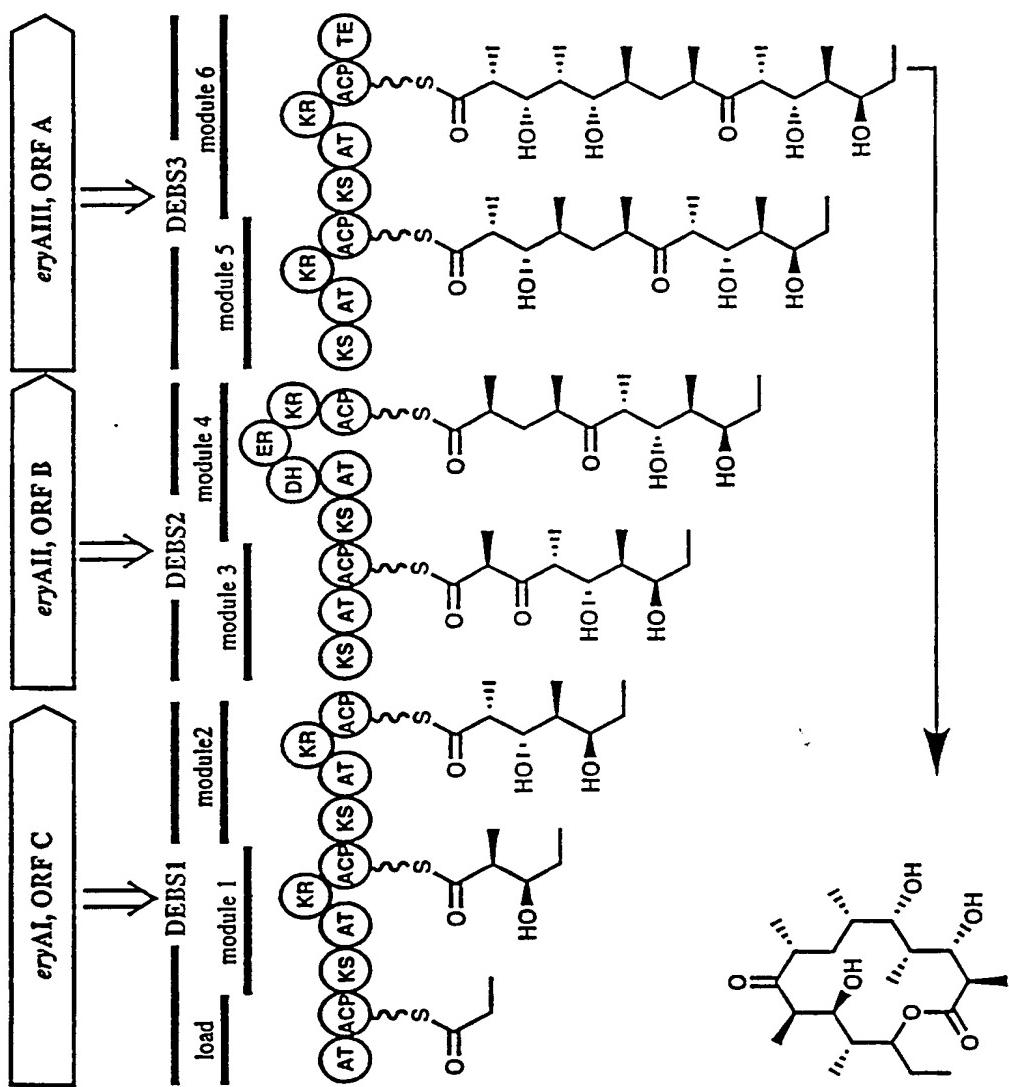


Fig. 1

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KCLFDAU -----MVTGLGIVAPNGLGVGAIWDAVLNGRNGIGPLR
KCLFPEU -----MTGTAARTASSQLHASPAGRRGLRGRAVVTGLGIVAPNGLGVGAYWDAVLNGRNGIGPLR
KCLFACT -----MSVLITGVGVVAPNGLGLAPYWSAVLDGRHGLGPVT
KCLFHIR -----MSTWWTGMGVVAPNGLGADDHWATLKGRHGISRLS
KCLFGRA -----MSTPDRRRAAVTGLSVAAPGGLGTERYWKSLLTGENGIAELS
KCLFNOG -----MTAAVVVTGLGVVAPTGLGVREHWSSTVRGASAIGPVT
KCLFTCM -----MSAPAPVVVTGLGIVAPNGTGTTEEYWAATLAGKSGIDVIQ
KCLFCIN -----MTP-VAVTGMGLAAPNGLGRPTTGRPPWAPRASAAST
KCLFVNZ -----MSASVVVTGLGVAAPNGLGREDFWASTLGGKSGIGPLT
KCLFWHIE -----MSGPQRTGTGGGSRRAVVTGLGVLSPHGTGVEAHKAVADGTSLGVPVT
KSGRA -----MTRRVVITGVGVRAVPGGSGTKEFWDLLTAGRTATRPI
KSHIR -----MTRRVVITGVGVRAVPGGLGAKNFWELLTSGRATATRRI
KSACT -----MKRRVVIITGVGVRAVPGGNGTRQFWELLTSGRATATRRI
KSCIN -----MTQRRAVITGIEVLAPOGGLGKRFWQLLSEGRTATRGIT
KSVNZ -----MTARRVVIITGIEVLAPOGCTGSKAFWNLLSEGRTATRGIT
KSNOG -----MKESINRRVVIITGIGIVAPDATGVKFWDLLTAGRTATRTIT
KSTCM -----MTRHAEKRVVIITGIGIVAPGGAGTAAFWDLLTAGRTATRTIS
KSDAU -----MNRRVVIITGMVVAPGAIGIKSFWELLSGTTATRAIT
KSPEU -----MNRRIVITGIGIVVAPGAVGKPFWELLSGTTATRAIS
KSWHI -----MTRRRVAVTIGIGIVVAPGGIGTPQFWRLLSEGRTATRRI
*: : * . *

KCLFDAU RFADDGRLGRLAGEVSDFVP-EDHLPKRLLVQTDPMTQMTALAAAEWALREAGCAPSS--
KCLFPEU RFTGDGRLGRLAGEVSDFVP-EDHLPKRLLAQTDPMTQY-ALAAAEWALRESGCSPSS--
KCLFACT RFDVSRYPATLAGQIDDFHA-PDHIPGRLLLQTDPMSTR-ALTAADWALQDAKADPES-L
KCLFHIR RFDPTGYPAELAGQVLDFA-TEHLPKRLLQTDVSTRF-ALAAAAWALADAEVDPAE-L
KCLFGRA RFDASRYPSSLAGQIDDFEA-SEHLPSSLRQTDVSTRY-ALAAAADWALADAGVGVPESGL
KCLFNOG RFDAGRYPSSLAGEVPGFVP-EDHLPSSLRQTDHMTRL-ALVAADWAFQDAAVDPSK-L
KCLFTCM RFDPHGYPVVGGEVLAFDA-AAHLPGRLLQTDRTMTQH-ALVAAEWAADAGLEPEK-Q
KCLFCIN RFDPSGYPAQLAGEIPGFRA-AEHLPGRLVPQTDRTVTRL-SLAAADWALADAGVEVAA-F
KCLFVNZ RFDPTGYPARLAGEVPGFAA-EEHLPSRLLQTDRTMTRL-ALVAADWALADAGVRPEE-Q
KCLFWHIE REGCAHPLRVAEGEVHGFDAAETVEDRFLVQTDRFTHF-ALSATQHALADARFGRADVD
KSGRA FFDASPPRSRIAGEI-DFDAVAEGFSPREVRRMDRATQF-AVACTRDALADSGLDTGAL
KSHIR FFDPTPNRSQIAAEC-DFDPHEGLSPREIRRMDRAAQF-AVVCTRDAVADSGLEFEQ-V
KSACT FFDPSPYRSQVAAEA-DFDPVAEGFGPRELDRMDRASQF-AVACAREAFAASGLDPDT-L
KSCIN FFDPAPFRSKVAAEA-DFCGLENLSPQEVRMDRAAQF-AVVTAR-AVEDSGAELAA-H
KSVNZ FFDPTPFRSRVAAEI-DFDPPEAHGLSPQEIRRMDRAAQF-AVVAAR-AVADSGIDLAA-H
KSNOG AFDPSPFRSRVAAEC-DFDPLAEGLTPQQIRRMDRATQF-AVVSARESLEDSGLDLGA-L
KSTCM LFDAAPYRSRIAGEI-DFDPPIGEGLSPRQASTYDRATQL-AVVCAREALKDSGLDPAA-V
KSDAU TFDATPFRSRVAAEC-DFDPVAAGLSAEQARRLDragQF-ALVAGQEAUTDGLRIGE-D
KSPEU TFDATPFRSRVAAEC-DFDPVAAGLSAEQARRLDragQF-ALVAGQEAULADGLRIDE-D
KSWHI LFDPSGLRSQIAAEC-DFEPSDHGLGLATAQRCDRYVQF-ALVAASEAVRDANLDMNR-E
*: : * . :

Fig 2A

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KCLFDAU - PLEAGVITASASGGFASGQRELQNLWSKG-----PAHVSAYMSFAWFY-AVNIGQIAIR
 KCLFPEU - PLEAGVITASASGGFASGQRELQNLWSKG-----PAHVSAYMSFAWFY-AVNIGQIAIR
 KCLFACT TDYDMGVVTANACGGFDFTREFRKLWSEG-----PKSVSVYESFAWFY-AVNIGQISIR
 KCLFHIR PEYGTGVITSNATGGFEFTREFRKLWAQG-----PEFVSVYESFAWFY-AVNIGQISIR
 KCLFGRA DDYDLGVVTSTAQGGFDFTREFRKLWSQG-----PAYVSVYESFAWFY-AVNIGQISIR
 KCLFNOG PEYGVGVVTASSAGGFEGFHRELQNLWSLG-----PQYVSAYQSFAWFY-AVNIGQVSIR
 KCLFTCM DEYGLGVLTAAAGAGGFEGFQREMQKLWGTG-----PERVSAYQSFAWFY-AVNIGQISIR
 KCLFCIN DPLDMGVVTASHAGGFEGFQDELQKLLQG-----QPVL SAYQSFAWFY-AVNSGQISIR
 KCLFVNZ DDFDMGVVTASASGGFEGFQGELQKLWSQG-----SQYVSAYQSFAWFY-AVNSGQISIR
 KCLFWHIE SPYSGVVTAAAGSGGGFEGFQRELQNLWGHG-----SRHVGPYQSIAWFY-AASTGQVSIR
 KSGRA DPSRIGVALGSAVASATSLENEYLVMSDSCREWLDPAHLSPPMFDFYLSPGVMPAEVAWA
 KSHIR PPERIGVSLGSAVAATSLQEYLVLDGGREWQVDPAYLSAHMFDYLSPGVMPAEVAWT
 KSACT DPARVGVSLGSAVAATSLEREYLLLSDSGRDWEVDAAWLSRHMFDFLYLPSSFAEVWA
 KSCIN PPHRIGVVVGSAVGATMGLDNEYRVVSDGGRLDLVDHYAVPHLYDYMVPSSFAEVWA
 KSVNZ DPYRUGVTVGSAVGATMGLDEEYRVVSDGGRLDLVDHYAVPHLYDYMVPSSFAEVWA
 KSNOG DASRTGVVVGSAVGCTTSLEEEYAVVSDSGRNWLVDGYAVPHLFDFYFVPSIICREVAWE
 KSTCM NPERIGVSI GTAVGCTTGLDREYARVSEGGSRWLVDHTLAQEQLFDYFVPTSIICREVAWE
 KSDAU SAHRVGVCVGTAVGCTOKLESEYVALSAGGAHWWVDPHRCAPELYDYFVPSLAAEVAWL
 KSPEU SAHRVGVCVGTAVGCTOKLESEYVALSAGGAHWWVDPGRGSPELYDYFVPSLAAEVAWL
 KSWHI DPWRAGATLGTAVGGTTRLEHDYVLVSERGSRWVDDDRSEPHLERAPTATLSAVAEE

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KCLFDAU - HDLRGPVGVVVAEQAGGLDALAHAR-RKVRRGAE-LIVSGAMDSSLCP-YGMAAQVRSG
 KCLFPEU - HDLRGPVGVVVAEQAGGLDALAHAR-RKVRRGAE-LIVSGAVDSSLCP-YGMAAQVKSG
 KCLFACT - HGMRGPSALVAEQAGGLDALGHAR-RTIRRGT-P-LVSGGVDSALDP-WGWVSQLIASG
 KCLFHIR - HGLRGPGSVLVAEQAGGLDAVGHG-AVRNGTP-MVVTGGVDSSFDP-WGWVSHVSSG
 KCLFGRA - NTMRGPSAALVGEQAGGLDAIGHAR-RTVRRGPG-WCSAVASTRSTR-GASSSQLSGG
 KCLFNOG - HGLRGPGGVLTIEQAGGLDALQAR-RQLRRGLP-MVVAQAVDGSPCP-WGWVAQLSSG
 KCLFTCM - HGMRGHSSVFITEQAGGLAAAHA-RLLRKGTNTALTGGCEASLCP-WGLVAQIPSG
 KCLFCIN - HGMKGPSPGVVSDQAGGLDALAQAR-RLVRKGTP-LIVCGAVEPRSPAGSPSSPAGG
 KCLFVNZ - NGMKGPSPGVVSDQAGGLDAVAQAR-RQIRKGTR-LIVSGVDASLCP-WGWVAHVASD
 KCLFWHIE - NDFKGPSPGVVAADEAGGLDALAHAA-LAVRNGTD-TVCGATEAPLAP-YSIVCQLGYP
 KSGRA - AGAEGPVTMVSDGCTSGLDSVGYAV-QGTREGSADVVVAGAADTPVSPIVVACFDAIKA
 KSHIR - VGAEGPVAMVSDGCTSGLDSLSHAC-SLIAEGTTDVMVAGAADTPITPIVVSCFDAIKA
 KSACT - VGAEGPVTMVSTGCTSGLDSVGNM-RAIEEGSADVMFAGAADTPITPIVVACFDAIRA
 KSCIN - VGAEGPSTVVSTGCTSGLDAVGIAV-ELVREGSVDVMVAGAVDAPISPPIP-CVLDIAKA
 KSVNZ - VGAEGPNTVVSTGCTSGLDSVGYARGELIREGSADVMIAGSSDAPISPITMACFDAIKA
 KSNOG RIGAEGPVSLVSTGCTSGLDAVGRAA-DLIAEGAADVMLAGATEAPIISPITVACFDAIKA
 KSTCM - AGAEGPVTVVSTGCTSGLDAVGYGT-ELIRDGRADVVVCCATDAPISPITVACFDAIKA
 KSDAU - AGAEGPVNIVSAGCTSGIDSIGYAC-ELIREGTVDVMLAGGVDAPIAPITVACFDAIRV
 KSPEU - AGAEGPVNIVSAGCTSGIDSIGYAC-ELIREGTVDAMVAGGVDAPIAPITVACFDAIRV
 KSWHI - FGVRGPVQTVSTGCTSGLDAVGYAY-HAVAEGRVDVCLAGAADSPISPITMACFDAIKA

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KCLFDAU RLSGSDDPTAGYLPDFDRAAGHVPGEG-GAILAVEDAERVAERG-GKVYGSIAGT-ASFDFD
 KCLFPEU RLSGSDNPTAGYLPDFDRAAGHVPGEG-GAILIVEDAERAERG-AKVYGSIAYGASFD
 KCLFACT RISTATDPDRAYLPFDERAAGYVPGEG-GAILVLEDAAAERGRHDAYGELAGCASTFD
 KCLFHIR RVSRATDPGRAYLPFDVAANGYVPGEG-GAILLLEDAAESAKARG-ATGYGEIAGYAATFD
 KCLFGRA LVSTVADPERAYLPFDAAAGGHVPGEG-GAVLIVEDADSARARG---AERIYVRSPLRRD
 KCLFNOG GLSTSDDPDRAYLPFDAAAGGHVPGEG-GALLVLESDESARARGVTRWYGRIDGYAATFD
 KCLFTCM FLSEATDPHDAYLPFDARAAGYVPGEG-GAMLVAERADSARERDAATVYGRAGHASTFD
 KCLFCIN -MSDSDEPNRAYLPFDRDGRGYVPGGGGRGVVPLEREAAPARG-AEVYGE-AGPLARL-
 KCLFVNZ RLSTSEEPARGYLPFDREAOQGHVPGEG-GAILVMEAAAERERG-ARIYGEIAGGSTFD
 KCLFWHIE ELSRATEPDRAYRPFTEAACGFAPAEG-GAVLVVEEEAAARERG-ADVRATVAGHAATFT

Fig 2B

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KSGRA	TTPRNDDPAHASRPFDGTRNGFVLAEG-AAMFVLEEEYAAQRRG-AHIYAEVGGYATRSQ
KSHIR	TTPRNDDPEHASRPFDNSRNGFVLAEG-AALFVLEELEHARARG-AHVYAEISGCATRLN
KSACT	TTARNDDEHASRPFDGTRDFVLAEG-AAMFVLEDYDSALARG-ARIHAEISGYATRCN
KSCIN	TPPRHDAPATASRPFDSTRNGFVLGEG-AAFFVLEELHSARRG-AHIYAEIAGYATRSN
KSVNZ	TTNRYDDPAHASRPFDGTRNGFVLGEG-AAVFVLEELESARARG-AHIYAEIAGYATRSN
KSONG	TPPRNDTPAEASRPFDRTNGFVLGEG-AAVFVLEEFEHARRG-ALVYAEIAGFATRCN
KSTCM	TSANNDPAHASRPFDNRDGFVLGEG-SAVFVLEELSAARRG-AHAYAEVRGFATRSN
KSDAU	TSDHNDTPETLA-PFSRSRNGFVLGEG-GAIVVLEEEAARVRG-ARIYAEIGGYASRGN
KSPEU	TSDHNDTPETASRPFSRSRNGFVLGEG-GAIVVLEEEAARVRG-ARIYAEIGGYASRGN
KSWHI	TSPNNDDPAHASRPFDADRGFVMGEG-AAVLVLEDLEHARARG-ADVYCEVSGYATFGN
* * * *	
KCLFDAU	-PPPGSGRP---SALARAVETALADAGLDRSDIAUVFADGAA-VGELDVAEAEALASVFG
KCLFPEU	-PPPGSGRP---SALARAVETALADAGLDGSIDIAUVFADGAA-VPELDAAEAEALASVFG
KCLFACT	-PAPGSGRP---AGLERAIRLALNDAGTGPEVDVVFADGAG-VPELDAAEARAIGRVFG
KCLFHIR	-PAPGSERP---PALRRAIELALADELRPEQDVVFADGAG-VAELDAIEAAAIRELFG
KCLFGRA	-PAPGSGRP---PALGRAELALAEAGLTPADISUVFADGAG-VPELDRAEADTLARLFG
KCLFNOG	-PPPGSGRP---PNLLRAAQALDDAEVGPEAVDVVFADASG-TPDDEDAEADAVRRLFG
KCLFTCM	-ARPCTGRP---TGPARAIIRLALEEARVAPEDDVWVYADAAG-VPALDRAEAEALAEVFG
KCLFCIN	-PAPHSGRG---STRAHAI RTALDDAGTAPGDIRRFAADGGGRYPN-DRAEAEAI SEVFG
KCLFVNZ	-PRPGSGRE---PGLRKAI ELALADAGAAPGIDUVVFADAAA-VPELDRVEAEALNAVFG
KCLFWHIE	GAGRWAESR-EGLARAI QGALAEAGCRPEEVDFVVFADALG-VPEADRAEALALADALG
KSGRA	-AYHMTGLKKDGREMAESIRALDEARLDRTAVDYVNAHGSG-TKQNDRHETAAFKRSLG
KSHIR	-AYHMTGLKTDGREMAEIRVALDLARIDPTIDYINAHGSG-TKQNDRHETAAFKRSLG
KSACT	-AYHMTGLKADGREMAETIRVALDESRTDATDIDYINAHGSG-TRQNDRHETAAYKRALG
KSCIN	-AYHMTGLR-DGAEMAIRLALDEARLNPEQVDYINAHGSG-TKQNDRHETAFFKALG
KSVNZ	-AYHMTGLRPDGAEMAEAIRVALDEARMNPEIDYINAHGSG-TKQNDRHETAFFKSLG
KSONG	-AFHMTGLRPDGREMAEAI GVALAQAGKAPADVDYVNAHGSG-TRQNDRHETAFFKRSLG
KSTCM	-AFHMTGLKPDGREMAEAITAALDQARRTGDDLHYINAHGSG-TRQNDRHETAFFKRSLG
KSDAU	-AYHMTGLRADGAEMAIAITAALDEARRDP SDVDYVNAHGTA-TRQNDRHETS AFKRSLG
KSPEU	-AYHMTGLRADGAEMAIAITAALDEARRDP SDVDYVNAHGTA-TKQNDRHETS AFKRSLG
KSWHI	-AYHMTGLTKEGLEMARAI DTALDMAELDGS AIDYVNAHGSG-TQQNDRHETA AVKRSLG
. : : * : : : * * : : : * :	

Fig 2C

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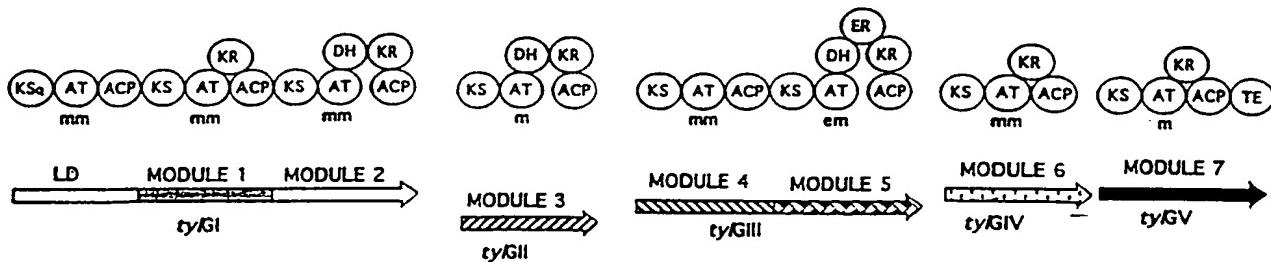
KCLFDAU	P--HRVPVTVPKTLTGRLYSGAGPLDVATGLLALRDEVVPATGHVH-PDPDPLPLDWTG
KCLFPEU	P--RRVPVTVPKTLTGRLYSGAGPLDVATALLALRDEVVPATAHD-PDPDPLPLDWTG
KCLFACT	R--BGPVTVPKTTIGRLYSGGGPLDVVTALMSLREGVIAPTAGTSVPREYGIDLVLGE
KCLFHIR	P--SGPVTAPKTMTGRLYSGGGPLDLVAALLAIRDGVIPPTVHTAEPVPERHOLDLVTD
KCLFGRA	P--RGVPVTAPKALTGRLCAGGGPADLAAALLALRDQVIPATGRHRAVPDAYALDLVTGR
KCLFNOC	P--YGVVPVTAPKTMTGRLSAGGAALDVATALLALREGVVPPTVNSRPRPEYELDLVLA-
KCLFTCM	P--GAVPVTAPEKTMGRLYAGGAALDVATALLSIRDCVVPPVTGAPAPGLGIDLVLHQ
KCLFCIN	P--GRVPVTCPRMTGRLHSGAAPLDVACALLAMRAGVIPPTVHID-PCPEYDLDLVLYQ
KCLFVNZ	T--GAVPVTAPEKTMGRLYSGAAPLDLAAAFLAMDEGVIPPTVNE-PDAAYGLDLVVGG
KCLFWHIE	PHAARVPVTAPKTGTGRAYCAAPVLDVATAVLAMEHGLIPPTPHVL-DVCHDLDLVTCR
KSGRA	EHAYAVPVSSIKSMGGHSLGAIGSIELAASVLAIEHNVPPPTANLHTPDPECDDYVPLT
KSHIR	EHAYRTPVSSIKSMVGHSLGAIGSIEVAACALAEHGVVPPPTANLHEPDPECDDYVPLT
KSACT	EHARRTPVSSIKSMVGHSLGAIGSLEIAACVLALEHGVVPPPTANLRTSDPECDDYVPLT
KSCIN	EHAYRTPVSSIKSMVGHSLGAIGSIEIAASALAMEYDVVPPPTANLHTPDPECDDYVPLT
KSVNZ	DHAYRTPVSSIKSMVGHSLGAIGSIEIAASALAMEHNVPPPTGNLHTPDPECDDYVR-S
KSONG	DHAYRVPVSSIKSMIGHSLGAIGSLEIAASVLAITHDVVPPPTANLHEPDPECDDYVPLR
KSTCM	QRADVPVSSIKSMIGHSLGAIGSLEIAACALAEHGVI PPTANYEEDPECDDYVPNV
KSDAU	DHAYRVPPISSVKSMIGHSLGAAGSLEVAATALAVEYGAIPPTANLHDPDPELDLDYVPLT
KSPEU	EHAYRVPPISSIKSMIGHSLGAVGSLEVAATALAVEYGVIPPTANLHDPDPELDLDYVPLT
KSWHI	EHAYATPMSSIKSVMVGHSLGAIGSIELAACVLAAMAHQVPPPTANYTTPDPECDDYVPL
.*:: : : *: . . : . : : . . : . * : * *	
KCLFDAU	PRAMADARAALVVARGHGGFNSALVVRGAA-----
KCLFPEU	PRSLADARAALLVARGYGGFNSALVVRGAA-----
KCLFACT	PRSTAPRTA-LVLARGRWGFNSAALVRRFAPTP----
KCLFHIR	PRHQQLGTA-LVLARLGKWFNSAVVVRGVIG-----
KCLFGRA	PREAALSAA-LVLARGRHGFNSAVVTLRGSDHRRPT
KCLFNOC	PRRTPLARA-LVLARGRGGFNAAMMAGPRAETR---
KCLFTCM	PRELRVDTA-LVVARGMGGFNSALVVRRHG-----
KCLFCIN	VRPAALRTA-LGGARGHGGFNSALVVRAQG-----
KCLFVNZ	PRTAEVNTA-LVIARGHGGFNSAMVVRSAN-----
KCLFWHIE	ARPAEPRTA-LVLARGLMGSNSALVLRRGAVPPEGR-
KSGRA	AREQRVDTV-LTVGSGFGGFQSAMVLHRPEEEA---
KSHIR	AREQRVDTV-LSVGSFGGFQSAMVLRRILGGANS--
KSACT	ARERKLRSV-LTVGSGFGGFQSAMVLRDAETAGAAA-
KSCIN	ARDQRVDSV-LTVGSGFGGFQSAMVLTSQ---RSTV
KSVNZ	CREQLTDSE-LTVGSGFGGFQSAMVLARPE---RKIA
KSONG	ARACPVDTV-LTVGSGFGGFQSAMVLCPGSRGRSAA
KSTCM	AREQRVDTV-LSVGSFGGFQSAAVLARPKETRS---
KSDAU	AREKRVRA-LTVGSGFGGFQSAMILLSRPER-----
KSPEU	AREKRVRA-LTVGSGFGGFQSAMILLSRLER-----
KSWHI	ARERTLRHV-LSVGSFGGFQSAVVLSGSEGGLR---

mole:- /ks2%

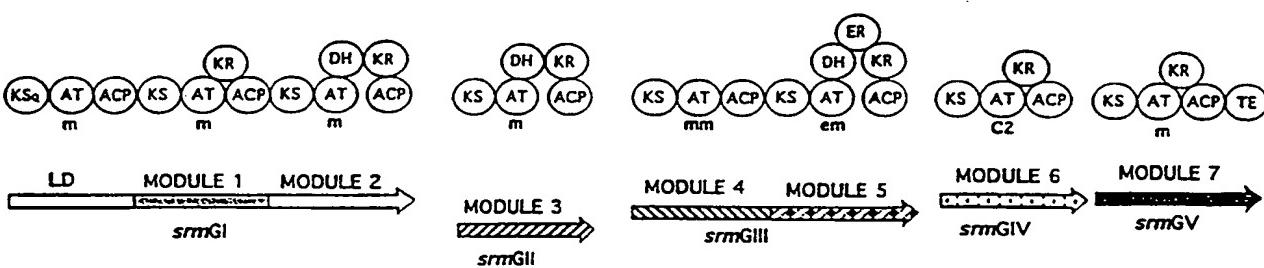
Fig 2D

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ORGANISATION OF THE TYLOSIN-PRODUCING POLYKETIDE SYNTHASE



ORGANISATION OF THE SPIRAMYCIN-PRODUCING POLYKETIDE SYNTHASE



ORGANISATION OF THE NIDDAMYCIN-PRODUCING POLYKETIDE SYNTHASE

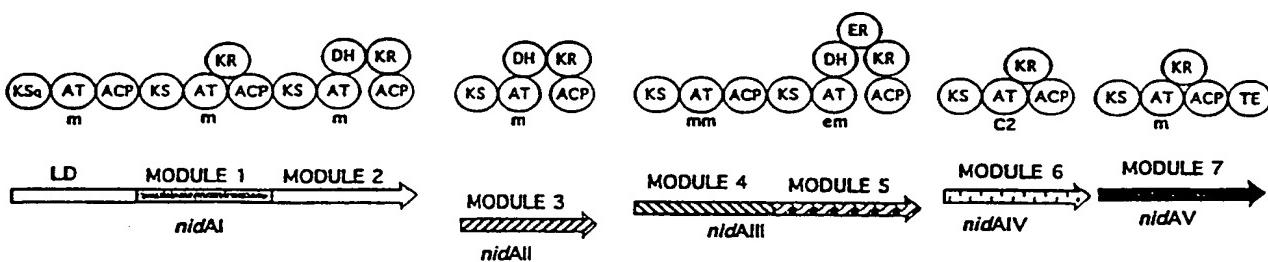


Fig 3

m: malonyl transferase
mm: methylmalonyl transferase
em: ethylmalonyl transferase
C2: unknown C2 unit transferase

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Fig. 4A

niddamycin	-----	-----	MAGHGDATAQ KAQDAEKSED GSDAIAVIGM	50
platenolide	-----	-----	MS GELAISRSDD RSDAVAVVGM	
monensin	-----	-----	MAAS ASASPSGPSA GPDPIAVVGM	
oleandomycin	-----	-----	MHVPGEE NGHSIAIVGI	
tylosin	MSSALRRAVQ	SNCGYGDLMT	SNTAAQNTGD QEDVDGPDST HGGEIAVVGM	
	51			100
niddam...	SCRFPGPAPGT	AEFWQLLSSG	ADAVVTAADG RRR.....	GTIDA
platenol.	ACRFPGPAPGI	AEFWKLLTDG	RDAIGRDADG RRR.....	GMIEA
monensin	ACRLPGAPDP	DAFWRLLSEG	RSAVSTAPPE RRRADSGLHG P...GGYLDR	
oleandom	ACRLPGSATP	QEFWRLLADS	ADALDEPPAG RFPTGSLSSP PAPRGGFLLDS	
tylosin	SCRLPGAAAGV	EEFWELLRSG	RGMPTRQDDG TWRAA.....	LED
	101			150
niddam...	PADFDAAFFG	MSPREAAATD	PQQRLVLELG WEALEDAGIV PESLRGEAAS	
platenol.	PGDFDAAFFG	MSPREAAETD	PQQRLMLELG WEALEDAGIV PGSLRGEAVG	
monensin	IDGFDADFFH	ISPREAVAMD	PQQRLLEELS WEALEDAGIR PPTLARSRTG	
oleandom	IDTFDADFFN	ISPREAGVLD	PQQRLALELG WEALEDAGIV PRHLRGTRTS	
tylosin	HAGFDAGFFG	MNARQAAATD	PQHRLMLELG WEALEDAGIV PGDLTGTDTG	
	151			200
niddam...	VFVGAMNDY	ATLLH.RAGA	PTDTYTATGL QHSMIANRLS YFLGLRGPSL	
platenol.	VFVGAMHDDY	ATLLH.RAGA	PVGPHATGL QRMLANRLS YVLGTRGPSL	
monensin	VFVGAFWDDY	TDVNLRAPG	AVTRHTMTGV HRSILANRIS YAYHLAGPSL	
oleandom	VFMGAMWDDY	AHLAHARGEA	ALTRHSLTGT HRGMIANRLS YALGLQGPSL	
tylosin	VFAGVASDDY	A.VLTRRSAV	SAGGYTATGL HRALAANRLS HFLGLRGPSL	
	201			250
niddam...	VVDTGQSSSL	VAVALAVESL	RGGTSGIALA GGVNLVLAEE GS.AAMERVG	
platenol.	AVDTAQSSSL	VAVALAVESL	RAGTSRVAVA GGVNLVLADE GT.AAMERLG	
monensin	TVDTAQSSSL	VAVHLACESI	RSGDSDIAFA GGVNLICSPR TTELAAARFG	
oleandom	TVDTGQSSSL	AAVHMACESL	ARGESDLALV GGVNLVLDPA GT.TGVERFG	
tylosin	VVDSAQSASL	VAVQLACESL	RRGETSLAVA GGVNLILTEE ST.TVMERMG	
	251			300
niddam...	ALSPDGRCHT	FDARANGYVR	GE GGAI VV LK PLADALADGD RVYCVVRGVA	
platenol.	ALSPDGRCHT	FDARANGYVR	GE GGAA VV LK PLADALADGD PVYCVVRGVA	
monensin	GLSAAGRCHT	FDARADGFVR	GE GGGL VV LK PLAAARRDGD TVYCVIRGSA	
oleandom	ALSPDGRCYT	FDSRANGYAR	GE GGVV VV LK PTHRALADGD TVYCEILGSA	
tylosin	ALSPDGRCHT	FDARANGYVR	GE GGGA VV LK PLDAALADGD RVYCVIKGGA	
	301			350
niddam...	TGNDGGGPGL	TVPDRAGQEA	VLRAACDQAG VR PADVRFVE LHGTGTPAGD	
platenol.	VGNDGGGPGL	TAPDREGQEA	VLRAACAQAR VDPAEVRFVE LHGTGTPVGD	
monensin	VNSDGTTDGI	TLPSGQAQQD	VVRLACRRAR ITPDQVQYVE LHGTGTPVGD	
oleandom	LNNDGATEGL	TVPSARAQAD	VLRQAWERAR VAPTDVQYVE LHGTGTPAGD	
tylosin	VNNNDGGGASL	TTPDREAQEA	VLRQAYRRAG VSTGAVRYVE LHGTGTRAGD	

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Fig 4B

800

niddam...	HG.GAMLSVQ AAEHDLDQLA HTHG..VEIA AVNGPTHCVL SGPRTALEET
platenol.	VG.GGMWSVG ASESVVRGVV EGLGEWSVA AVNGPRSVVL SGDVGVLESV
monensin	AP.GAMAAWQ ATADEAAEQL AGHERHVTVA AVNGPDSVVV SGDRATVDEL
oleandom	GG.GVMLSVQ APESEVAPLL LGREAHVGLA AVNGPDAVVV SGERGHVAAI
tylosin	AGRGAAMAAPP LPAGEVEAGL AKWPGVEVA AVNGPASTVV SGDRRAVAGY

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850

niddam...	AQHLREQNVR HTWLKVSHAF HSALMDPMLG AFRDTLNLTN Y..QPPTIPL
platenol.	VASLMGDGVE YRRLDVSHGF HSVLMEPVLG EFRGVVESLE FGRVRPGVVV
monensin	TAAWRGRGRK AHHLKVSHAF HSPHMDPILD ELRAVAAGLT FHE..PVIPV
oleandom	EQILRDRGRK SRYLRVSHAF HSPLMEPVLE EFAEAAVAGLT FRA..PTTPL
tylosin	VAVCQAEGVQ ARЛИPVDYAS HSRHVEDLKG ELERVLSGI. RPRSPRVPV

851

900

niddam...	ISNLTGQIA.DPNHL CTPDYWIDHA RHTVRFADAV QTAHHHQGTTT
platenol.	VSGVSGGVV.GSGEL GDPGYWVRHA REAVRFADGV GVVRLGVGT
monensin	VSNVTGELVT ATATGSGAGQ ADPEYWARHA REPVRFLSGV RGLCERGVTT
oleandom	VSNLTG.... APVDDRTM ATPAYWVRHV REAVRGDG1 RALGKLGTGS
tylosin	CSTVAGEQPG EPVF..... DAGYWFRNL RNRVEFSAVV GGLLEEGHRR

901

950

niddam...	YLEIGPHPTL TTLLHHTL.. DNP..... T TIPTLHRERP
platenol.	LVEVGP HGVL TGIMAGECLGA GDDV..... V VVPAMRRGRA
monensin	FVELGP DAPL SAMARDCFPA P..... ADRSRPRPA AIATCRRGRD
oleandom	FLEVGP DGVL TAMARACVTA APEPGHRGEQ GADADAHTAL LLPALRRGRD
tylosin	FIEVSAHPV L V..... HAIEQ TAAEADRSVH ATGTLRRQDD

951

niddam...	EPETLTQAI A AVGVRTDGID WAVLCGASRP RRVELPTYAF
platenol.	EREVFEAALA TVFTRDAGLD ATALHTGSTG RRIDLPTTPF
monensin	EVATFLRSLA QAYVRGADVD FTRAYGATAT RRFPLPTYPF
oleandom	EARSLTEAVA RLHLHGVPMD WTSVLGGDVS .RVPLPTYAF
tylosin	SPHRLLTSTA EAWAHGATLT WDPAL..PPG HLTTLPTYPF

niddam: niddamycin; platenol: platenolide I (spiramycin); oleandom: oleandomycin.

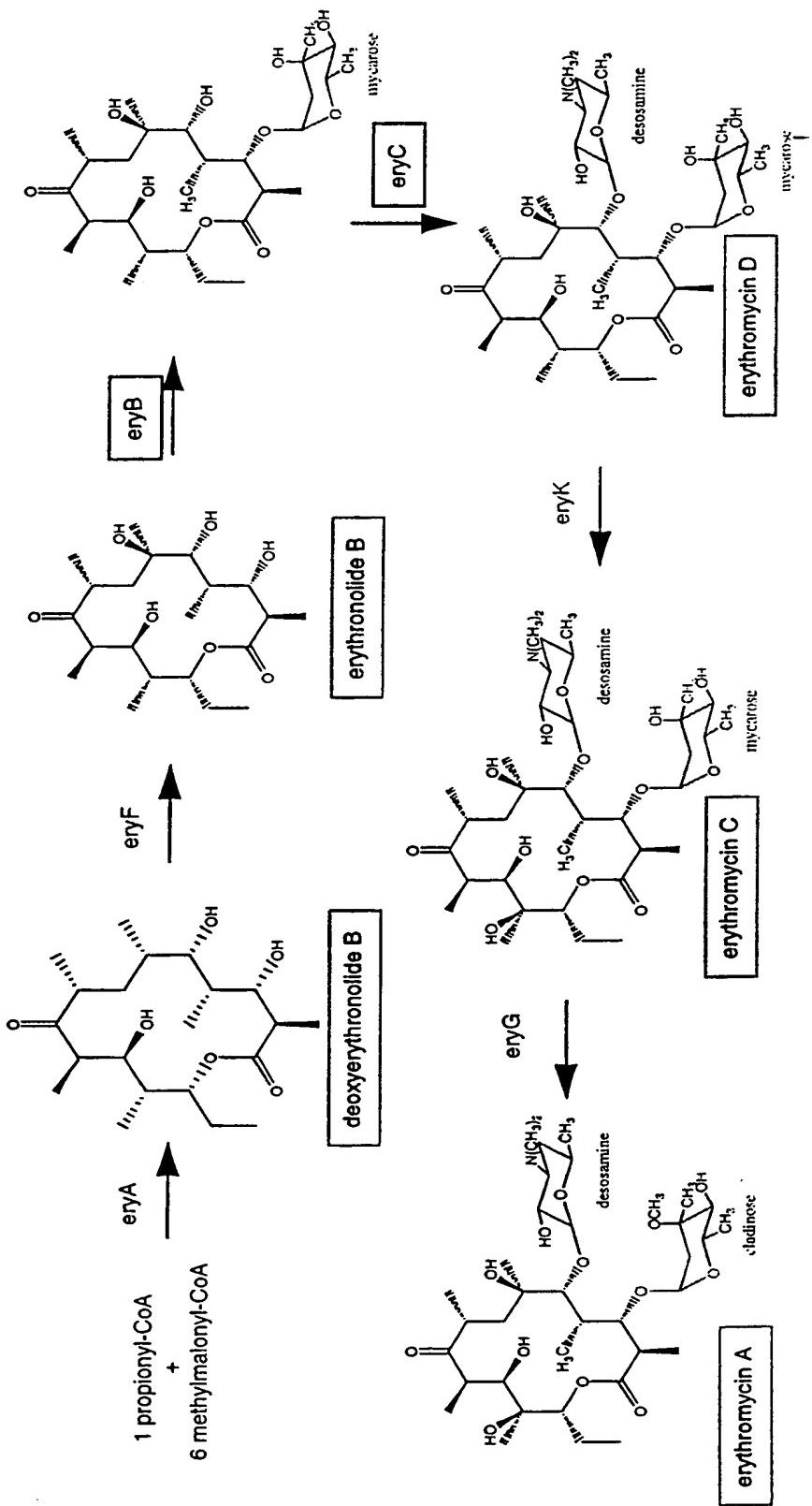
FIG. 4C

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**Fig. 5**

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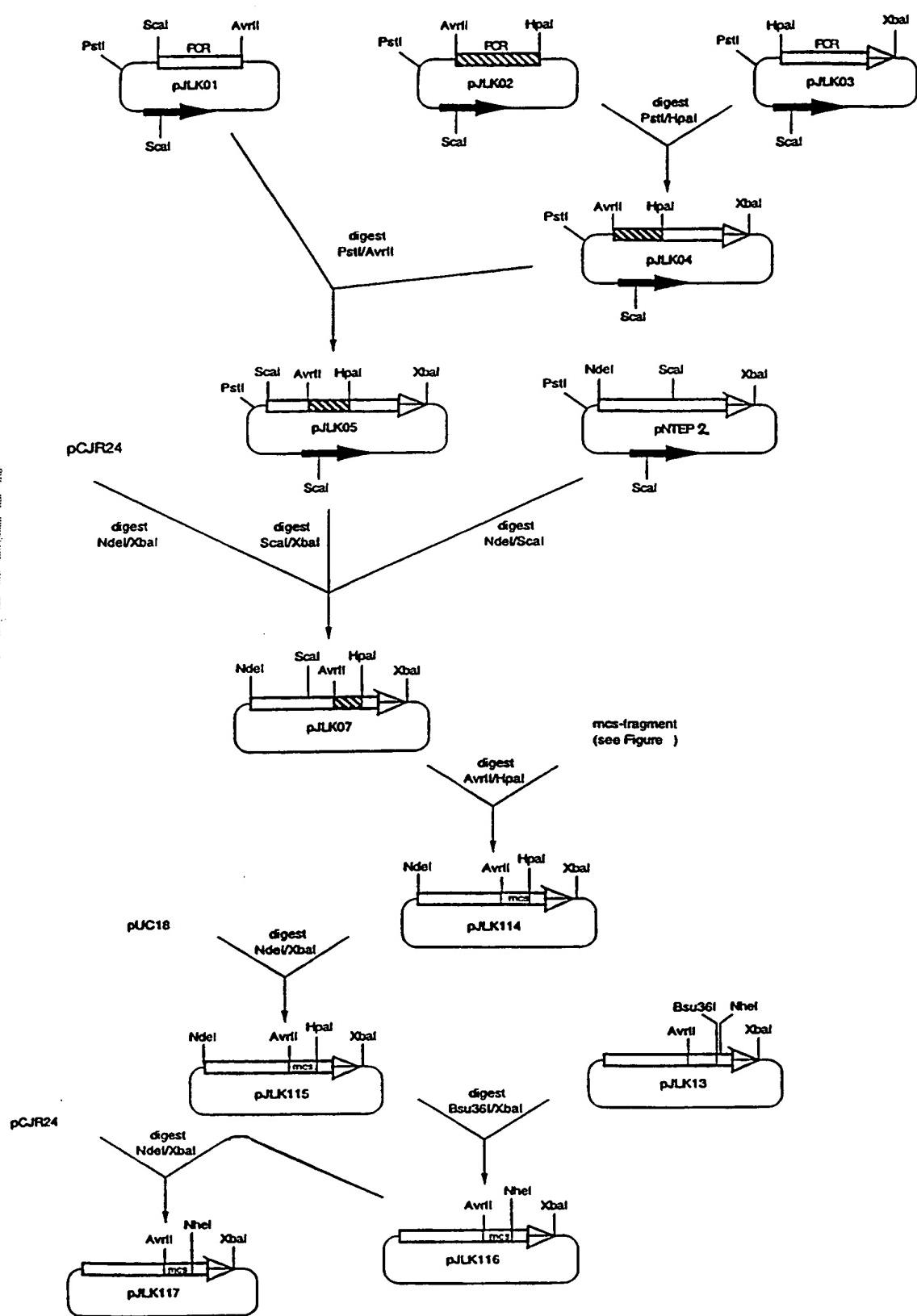


Fig 6

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Figure 7

forward (P1f) :

5'-CTA GGC CGG GCC GGA CTG GTA GAT CTG CCT ACG TAT CCT TTC CAG GGC AAG CGG TTC TGG CTG CAG CCG GAC CGC ACT AGT CCT CGT GAC GAG
 GGA GAT GCA TCG AGC CTG AGG GAC CGG TT-3'

backward (P1b) :

5'-AAC CGG TCC CTC GAT GCA TCT CCC TCG TCA CGA GGA CTA GTG CGG TCC GCC AGC AAC CGC TTT CCC TGG AAA GGA TAC GTA
 GGC AGA TCT ACC AGT CCG GCC CGG C-3'

oligos annealed:

CTAGGCCGGCCGGACTGGTAGATCTGGCTAACGTGGCTGGGAAAGGGGGTCTGGCTGCGGACTGGGAGATGGCATGGCTTGCGGACCGGTT
 CGGCCCGGCCCTGACCATCTAGACGGATGCAATGGAAAGGTCCCCTACGTAGCTGGACTGCTCCCTACGTAGCTGGACTCTACGTAGCTGGCAA

 AvrII BglII SmaI PstI SpeI NsiI Bsu36I HpaI